the Patent Office is authorized to charge the underpayment to Deposit Account No. 04-1073.

AMENDMENTS

In the Claims:

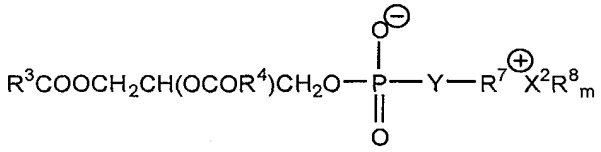
Please cancel claim 1 without prejudice.

Please add new claims 21-49 pursuant to 37 C.F.R. § 1.121(c)(1)(i) as set forth in the "clean" version set forth below. Entry is respectfully requested.

21(NEW). An oral vaccine comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components and comprising

a) at least one cationic compound;

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are a group of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_f(CH_2)_g$- in which f is 0 to 6, each of e and g are 0 to 23 and e + g and 3f is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^2 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms,

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0:

in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

22(NEW). A vaccine according to claim 21 in which the cationic compound has the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6_n \qquad I$$

in which R^1 and R^2 are the same or different and are a group of the formula $CH_3(CH_2)_a(CH{=}CH\text{-}CH_2)_b(CH_2)_c(CO)_d$- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-12} aryl and aralkyl, or two or three of the groups R^6 together with X^1 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

23(NEW). A vaccine according to claim 22 in which R^1 is the same as R^2 and R^3 is the same as R^4.

24(NEW). A vaccine according to claim 23 in which R^1 and R^2 represent a different group to R^3 and R^4.

25(NEW). A vaccine according to claim 23 in which R^1 and R^2 represent a different group to R^3 and R^4 , and in which in R^1 and R^2, b is 1, and in which (a + c) is in

the range 10 to 20.

26(NEW). A vaccine according to claim 23 in which d is 0.

27(NEW). A vaccine according to claim 22 in which X^1 is N and in which the R^6 groups are all C_{1-4} alkyl.

28(NEW). A vaccine according to claim 21 which comprises two zwitterionic phospholipids in each of which Y is O, X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid are all C_{1-4} alkyl.

29(NEW). A vaccine according to claim 28 in which, in each phospholipid R^7 is $(CH_2)_h$ in which h is 2 or 3.

30(NEW). A vaccine according to claim 28 in which the groups R^3 and R^4 of the said first phospholipid are the same and each is a group in which f is1 and (e + g) is in the range 10 to 20.

31(NEW). A vaccine according to claim 30 in which in the groups R^3 and R^4 of the said second phospholipid are the same, f is O and e + g is in the range 15 to 23.

32(NEW). A vaccine according to claim 31 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

33(NEW). A vaccine according to claim 21 in which the cationic compound is cholesterol-3β-N-(dimethyaminoethyl) carbamate.

34(NEW). An oral vaccine according to claim 21 in which the liposome forming components include at least 25 mole% of components which individually have a transition temperature of more than 40°C.

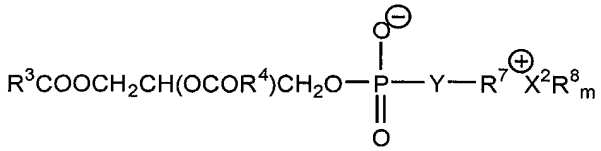
35(NEW). A vaccine according to claim 21 in which the nucleic acid is entrapped within the liposomes.

36(NEW). A method of entrapping polynucleotide into liposomes involving the steps of:

i) forming an aqueous suspension comprising naked nucleic acid, which operatively encodes an immunogenic polypeptide useful to induce a desired immune response in a human or animal subject, and preformed liposomes formed of liposome forming components comprising

a) at least one cationic compound;

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are selected from groups of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_f(CH_2)_g$- in which f is 0 to 6, each of e and g are 0 to 23 and e + g and 3f is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, $C_{1\text{-}8}$ alkyl, $C_{6\text{-}11}$ aryl or aralkyl, or two or three of the groups R^8 together with X^2

form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms,

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0:

in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

ii) freeze-drying or spray-drying the suspension, and

iii) rehydrating the product of step ii) to form dehydration/rehydration vesicles.

37(NEW). A method according to claim 36 comprising the further steps of:

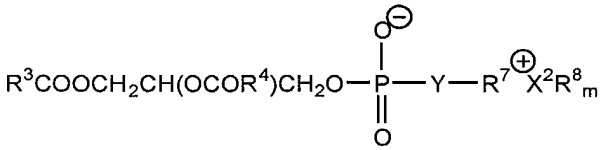
iv) subjecting the aqueous suspension of dehydration/rehydration vesicles from step iii to microfluidization to control their size; and

v) optionally separating non-entrapped nucleic acid from liposomes.

38(NEW). Method of vaccinating an animal comprising administering orally a composition comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components comprising

a) at least one cationic compound

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are a group of the formula $CH_3(CH_2)_e(CH{=}CH{-}CH_2)_g{-}$ in which f is 0 to 6, each of e and g + 3f are 0 to 23 and e + g is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^2 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms;

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0,

wherein the molar ratio of cationic compound to zwitterionic phospholipid is in the range 1:1 to 1:10,

whereby an immune response to the said antigen is generated.

40(NEW). A method according to claim 38 in which the cationic compound has the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6{}_n \qquad I$$

in which R^1 and R^2 are the same or different and are a group of the formula $CH_3(CH_2)_a(CH{=}CH\text{-}CH_2)_b(CH_2)_c(CO)_d$- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-12} aryl and aralkyl, or two or three of the groups R^6 together with X^1 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

41(NEW). A method according to claim 40 in which R^1 is the same as R^2 and R^3 is the same as R^4.

42(NEW). A method according to claim 41 in which R^1 and R^2 represent a

different group to R^3 and R^4.

43(NEW). A method according to claim 41 in which R^1 and R^2 represent a different group to R^3 and R^4 , in which in R^1 and R^2, b is 1, and in which (a + c) is in the range 10 to 20.

44(NEW). A method according to claim 38 in which the liposome forming materials comprise two zwitterionic phospholipids in each of which Y is O, X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid are all C_{1-14} alkyl, and R^7 is $(CH_2)_h$ in which h is 2 or 3.

45(NEW). A method according to claim 44 in which the groups R^3 and R^4 of the said first phospholipid are the same and each is a group in which f is 1 and (e + g) is in the range 10 to 20.

46(NEW). A method according to claim 45 in which in the groups R^3 and R^4 of the said second phospholipid are the same f is 0 and e+ g is in the range 15 to 23.

47(NEW). A method according to claim 46 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

48(NEW). A method according to claim 38 in which the cationic compound is cholesterol-3β-N-(dimethyaminoethyl) carbamate.

49(NEW). A method according to claim 38 in which the nucleic acid is entrapped within the liposomes.